Virginia Department of Health
Glanders: Guidance for Health Care Providers
Key Medical and Public Health Interventions

Glanders is a zoonotic disease caused by the bacterium *Burkholderia mallei* (formerly *Pseudomonas mallei*). Glanders is primarily a disease of equids (horses, donkeys and mules), but may infect humans. Transmission from infected animals to humans is rare, and no human epidemics of glanders have been reported, suggesting that glanders is not easily transmissible from animal-to-human or from human-to-human. Human infection occurs through direct mucous membrane contact with infected animal materials, direct contact of abraded or lacerated skin with infected animal materials, or inhalation of infective aerosols. In the laboratory setting, infection may occur through direct mucous membrane or skin contact with *B. mallei* cultures or through inhalation of infective aerosols.

1. Clinical Manifestations

Incubation period: 1-14 days (may vary depending on route of infection)
Signs and Symptoms: Vary with the form of disease

Localized: May be limited to skin ulceration at the site of bacterial entry, with symptoms usually occurring 1-5 days after exposure. Subsequent symptoms may include nodules, abscesses, and/or ulcers in skin, mucous membranes, lymphatic vessels, and/or subcutaneous tissues; mucopurulent discharge from mucous membranes; or lymphadenopathy. Localized infection may disseminate. Manifestations of systemic invasion include a diffuse papular and/or pustular rash, hepatic and/or splenic abscesses, pulmonary lesions or septic shock.

Septicemia: May include fever, chills, myalgia, pleuritic chest pain, generalized erythroderma, jaundice, lacrimation, diarrhea, granulomatous or necrotizing lesions, hepatomegaly, splenomegaly or cervical adenopathy. Untreated glanders septicemia results in death in 95% of cases; with treatment, death occurs in greater than 50% of cases. Note: blood cultures often remain negative.

Pulmonary: May include cough, fever, dyspnea, mucopurulent discharge, pulmonary abscesses, pleural effusions, skin abscesses after several months or symptoms as described above for septicemia. If inhalation is the primary route of infection, signs and symptoms usually appear within 10-14 days.

Chronic: May include multiple abscesses, nodules, or ulcers in the skin, liver, spleen or muscles of the arms and legs. Associated enlargement and induration of regional lymph nodes and channels may occur. Characterized by remission and exacerbation.

2. Identification and Isolation of Cases

Aggressive identification and elimination of animals infected with *B. mallei* has essentially eliminated glanders from the U.S. Other than a confirmed case of glanders in 2000 in a microbiologist who worked with cultures of *B. mallei*, no human cases have been reported in the U.S. since the 1940s. However, glanders remains endemic in parts of Asia, the Middle East, Africa, and Central and South America.

If a case of glanders is suspected, it is critical to identify the individual's occupation (e.g., laboratory worker, veterinarian, or any job involving equids) and travel history to assess possible exposures. If the patient's history does not indicate a possible source of exposure, bioterrorism should be suspected. *B. mallei* is considered a CDC Category B bioterrorism agent. If used for bioterrorism, the bacteria would likely be delivered as an aerosol, which is considered to be highly infectious to humans.

For infection control, standard precautions are adequate for most patients with suspected glanders. Additional precautions may be necessary depending on the form of disease or the specific area(s) of the body involved. For example, for patients with draining cutaneous lesions or mucopurulent nasal discharge, contact precautions are indicated.

3. Handling Laboratory Specimens

Because *B. mallei* is highly infectious in the laboratory, laboratory personnel should be alerted when glanders is suspected to ensure safe and appropriate specimen processing. Consultation with the Division of Consolidated Laboratory Services (DCLS) is strongly recommended. The DCLS Emergency Services Officer can be paged 24 hours a day/7 days a week at (804) 418-9923.

When *B. mallei* is suspected, it is recommended that all microbiology laboratory work be performed in a biosafety cabinet within a BSL-3 laboratory. An acceptable alternative is to work within a biosafety cabinet located within a BSL-2 laboratory while utilizing BSL-3 work practices, such as wearing gowns and gloves. In addition, culture plates should be taped shut during incubation and anytime the culture plates are located outside the biosafety cabinet.

Because *B. mallei* is rarely isolated in the United States, its characteristics are unfamiliar to many clinical microbiologists. Commercial bacterial identification systems may misidentify *B. mallei*. Therefore, any isolate should be referred to DCLS if it meets the following identification criteria suspicious for *B. mallei*:

- **A.** Colony morphology on sheep blood agar: colonies appear smooth, gray, or translucent after 48 hours of incubation.
- **B.** Gram stain morphology: Gram negative, faintly staining, straight or slightly curved coccobacilli
- **C.** Oxidase test: variable result
- **D.** Motility test: non-motile
- **E.** Growth at 42 degrees C on sheep blood agar: very light growth at 72 hours
- **F.** Triple Sugar Iron (TSI): non-fermenter

DCLS clinical sample collection instructions are shown in Table 1. Consultation with DCLS is required before specimen collection and submission.

Table 1. Sample Collection for Suspected Glanders

Specimen	*Amount*	*Instructions*
Blood (for culture)	10 ml	Collect in blood isolator tube or aerobic blood culture bottle. Ship at room temperature. Transport to lab within 16 hours.
Blood or serum	2 ml (or more)	Collect blood in red top or EDTA tube. Ship refrigerated. Transport to lab as soon as possible.
Urine	10 ml (or more)	Collect a midstream clean-catch or catheterized specimen in a sterile screw-capped leak-proof container. Ship refrigerated. Transport to lab as soon as possible.
Abscess, tissue aspirate, or purulent discharge	3 ml, or as much material as possible (avoid swabs)	Aspirate with a syringe and transfer material to a sterile screw-capped leak-proof container, if possible. Aspirate can remain in collection syringe if needle is removed and syringe is capped to prevent leakage. Ship refrigerated. Transport to lab as soon as possible.
Sputum, deep or induced	3 ml (or more)	Collect in sterile screw-capped leak-proof container. Ship refrigerated. Transport to lab as soon as possible.
Tissue biopsy	1 gram	Collect in sterile container. Moisten sample with sterile broth or saline. Ship refrigerated. Transport to lab as soon as possible.
Bacterial isolate from culture		Ship suspicious bacterial isolates on agar slant at room temperature.

Additional laboratory guidance is available in the publication "Sentinel Laboratory Guidelines for Suspected Agents of Bioterrorism. *Burkholderia mallei* and *B. pseudomallei*" available at the American Society for Microbiology website at http://www.asm.org/Policy/index.asp?bid=6342.

4. Diagnosis

There is currently no CDC case definition for glanders. Isolation of *B. mallei* from a clinical sample with definitive identification at DCLS and/or CDC in conjunction with clinically compatible signs and symptoms should guide treatment and public health measures. Blood cultures often remain negative, even in patients with septicemia.

5. Treatment and Prophylaxis

Treatment: There are currently no standard recommendations for glanders treatment, in part because there has been little clinical experience in treating glanders in the antibiotic era. *In vitro* antibiotic susceptibility profiles for *B. mallei* resemble those of *B. pseudomallei*, the causative agent of meliodosis, for which there is recent clinical experience. Treatment recommendations for glanders, therefore, are based on *in vitro* antibiotic susceptibility profiles for *B. mallei* and clinical experience in the treatment of meliodosis.

Adult patients with glanders should be treated initially with a 2 week parenteral regimen of:

- ceftazidime [50 mg/kg (max: 2 g) every 6 hours]*, **or**
- imipenem [25 mg/kg (max: 1 g) every 6 hours]*, **or**
- meropenem [25 mg/kg (max: 1 g) every 8 hours]*

and (optional)

- TMP-SMX [8 mg/kg TMP and 40 mg/kg SMX (max: 320 mg TMP/1,600 mg SMX) every 12 hours]*

Following the two weeks of parenteral antibiotic treatment, prolonged (at least 3 months) antibiotic treatment with oral TMP-SMX [8 mg/kg TMP and 40 mg/kg SMX (max: 320 mg TMP/1,600 mg SMX) every 12 hours]*, **and (optional)** oral doxycycline [2 mg/kg (max: 100 mg) every 12 hours] is recommended to ensure complete eradication of the organism.

Since there is little clinical experience in treating glanders and *B. mallei* as a bioterrorism agent may be genetically modified, treatment should be adjusted according to clinical response and susceptibility profiles of clinical isolates. Treatment decisions should be made in close consultation with the patient's physician, infectious disease specialists, and public health professionals.

Prophylaxis: Post-exposure prophylaxis is of unproven benefit. However, in the event of a known high risk exposure, post-exposure prophylaxis may be attempted with oral TMP-SMX [8 mg/kg TMP and 40 mg/kg SMX (max: 320 mg TMP/1,600 mg SMX) every 12 hours]* **or** oral doxycycline [2 mg/kg (max: 100 mg) every 12 hours].

***NOTE: Dosage reduction for these antibiotics is required in patients with impaired renal function.*

6. Vaccine

There is no vaccine for glanders, although research in glanders vaccine development is in progress.

7. Decontamination

Normally *B. mallei* does not survive when dried or heated.

Potentially contaminated material should be cleaned with a solution of 1 part household bleach to 9 parts water (0.5% sodium hypochlorite solution). Hospital rooms of patients with glanders should receive terminal cleaning consistent with standard precautions, and clothing or linens contaminated with body fluids should be disinfected according to hospital protocol.

8. Postmortem Practices

If glanders is suspected as a cause of death, the district Office of the Chief Medical Examiner (OCME) should be notified immediately. Consult with OCME to determine if an autopsy should be conducted, the parties responsible for conducting the autopsy and the appropriate personal protective procedures to follow.

9. Public Health Measures

A. Suspected cases should be reported to hospital epidemiology/infection control, who in turn should notify laboratory personnel, other medical care providers, and the local health department. The local health department should immediately notify the Division of Surveillance and Investigation (DSI) or the Division of Zoonotic and Environmental Epidemiology (DZEE) in the central office of the Virginia Department of Health (VDH) about the suspect case. DSI or DZEE staff can be reached during work hours at (804) 864-8141 or on the VDH emergency phone at (866) 531-3068 after work hours, at night and on weekends.
B. Clinical specimens and/or isolates of *B. mallei* should be sent to DCLS for confirmation of the agent and other studies. The DCLS Emergency Services Officer can be paged 24 hours a day/7 days a week at (804) 418-9923.
C. Designated public health authorities should begin an epidemiologic investigation to include the following:
    a. Collection of detailed information from the patient (or his/her designee) about possible exposures (including occupational and travel history).
    b. Investigation of contacts of the case for compatible illness that may be due to a common exposure.
    c. Notification of the Virginia Department of Agriculture and Consumer Services if animal exposures are identified.

References

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